Abstract ASHG – GWAS of skin prick tests

Identification of common and specific genetic determinants to skin prick test reactivity using genome-wide association study and gene-based test approaches

P-E. Sugier1,2,3, A. Vaysse1,2,3, C. Loucoubar1,2,3, C. Sarnowski1,2,3, P. Margaritte-Jeannin1,2,3, M-H. Dizier1,2,3, M. Lathrop3,4, F. Demenais1,2,3, E. Bouzigon1,2,3, and the EGEA collaborative group

1INSERM, U946, France
2Université Paris Diderot, Sorbonne Paris Cité, Institut Universitaire d’Hématologie, France
3Fondation Jean Dausset-Centre d’Etude du Polymorphisme Humain (CEPH), France
4CEA-CNG, France

The prevalence of allergic diseases such as asthma has reached pandemic proportions in industrialized countries. The genetic component of allergy is substantial but it has been rarely investigated at the genome-wide level. Two genome-wide association studies (GWAS) of atopy defined as increased specific IgE levels or skin prick test (SPT) reactivity to allergens have been conducted in population-based cohorts with inconsistent results.

We aimed to identify common and specific genetic determinants of SPT response to a panel of aeroallergens using a GWAS approach combining a single SNP analysis followed by gene-based association tests.

We conducted GWAS of atopy phenotypes in 1,660 subjects (925 atopics and 735 non-atopics) from the French Epidemiological study on the Genetics and Environment of Asthma (EGEA) which includes families ascertained through asthmatics. These subjects were genotyped by Illumina 610K Array. Four atopy traits were investigated: 1) atopy as a whole and defined by a positive SPT response to at least one of 11 aeroallergens, and then three groups of aeroallergens: 2) indoors (Dermatophagoides pteronyssinus, cat, Blattella germanica), 3) outdoors (timothy grass, olive, birch, Parietaria judaica, ragweed), and 4) molds (Cladosporium herbarum, Aspergillus, Alternaria tenuis).

For each phenotype, a single SNP analysis was performed across the genome followed by gene-based association tests using VEGAS (Lui et al Am J Hum Genet 2010).

Six atopy loci were detected at P-value≤5x10−7 by single SNP analyses. One gene in 3q24 region was strongly associated to atopy as a whole (P=3x10−7) and in a lesser extend to each SPT group (P ranging from 5x10−6 to 3x10−4), suggesting this locus harbor common genetic determinant shared across SPT response to allergens. Five loci were mainly detected in sub-groups of allergens: 5q13 with indoors, 12q24 with outdoors and 4q24, 15q13 and 19q13 with molds. Gene-based tests both strengthened the evidence for association of 19q13 locus with SPT to molds and increased evidence for two other loci on chromosome 19 with this phenotype.

Further investigation will be needed to confirm our findings in order to reliably identify key genetic factors underlying atopy predisposition. This study highlights that combining at the genome-wide level single SNP analyses and gene-based tests may facilitate the identification of new susceptibility genes.

Funded by INSERM, French Min Education & Research, ANR-GWIS-AM

No characters: 2478
/ 2486 avec caractères spéciaux